THE INFLUENCE OF THE PITUITARY ON BASAL METABOLISM AND ON SPECIFIC DYNAMIC ACTION

B. A. HOUSSAY
Institute of Physiology, Faculty of Medicine
BUENOS AIRES

The influence of the pituitary on basal metabolism has been frequently studied in our Institute, papers having been published on the subject in 1930, 1931, 1932 and 1933. In these (1, 9) the bibliographical references on the investigations in different species are to be found.

Most of the experiments in this series have been performed in the dog as has been most of our work on the pituitary, as we wished to make a deeper analysis of the facts in one species. The animals were trained to keep quiet and motionless without anaesthesia or being tied during the tests (1, 2, 10, 11, 17). The air expired during 20 to 30 minutes was analyzed with Haldane's burette. The calories produced were calculated from the oxygen consumed, taking into account the R.Q., and in all cases expressed per square metre per 24 hours. The experimental details are set forth extensively in the papers referred to in the bibliography.

Up to the present the basal metabolic determinations of 27 hypophysectomized dogs have been published, 22 of which were performed in our Institute (several determinations having been made for each dog, 1, 10, 17). In each one of our series the average of basal determination in the hypophysectomized animals was 13 to 16 per cent less than in the controls. The average is —16 per cent for the 27 known cases (see Table 1). The extreme

TABLE 1

BASAL METABOLISM IN NORMAL DOGS

Author	No. of Dogs	Cals./sq. m./day	Author	No. of Dogs	Cals./sq. m./day
Rubner	8	973	Gaebler	1	816
Lusk, Du Bois	11	772	Rapport, Beard	1	784
Kunde	7	777	Plummer, Deuel, Lusk	1	763
Kunde, Steinhaus	7	760	Artundo	5	791
Boothby, Sandiford	4	941	Mazzocco	9	888
Hesse	4	800	Houssay, Artundo	5	804

BASAL METABOLISM IN HYPOPHYSECTOMIZED DOGS

Author	No. of Dogs	Cals./sq. m./day	Author	No. of Dogs	Cals./sq. m./day	Per Cent of the Controls
Benedict, Homans	3	700	Artundo (1930)	8	666	—15.8
Aschner, Porges	1	550	Mazzocco (1932)	9	745	—16.
Gaebler	1	795	Houssay, Artundo (1933)	5	702	—12.6

Average of 27 dogs: 703 cal./sq. m./day. —16 per cent of normal.
In 22 (81%) B. M. was low; in 5 (19%) B. M. was normal or high.

individual values in the hypophysectomized cases were 469 and 931 calories per square metre per 24 hours, but the value was low in 22 (81 per cent) and normal or high in only 5 (19 per cent).

This moderate decrease, very frequent but not constant, of the basal metabolism could be due in hypophysectomized animals either to the alteration in the thyroid function or to the suppression of a pituitary hormone acting directly on the basal metabolic rate.

The thyroid of hypophysectomized dogs shows morphological and functional signs of hypofunction (1, 2, 3). The weight of the gland is decreased, the epithelium low and flattened, almost endothelial; the cells are small, the vesicles of normal width appear dilated, colloid is dense with no central vacuoles and few at the periphery. There are no zones of functional activity as in normal thyroids. After subtotal thyroidectomy compensatory hypertrophy is not produced. Sometimes the walls of the acini break down and large vesicles are so formed. This picture of permanent and intense atrophy is preceded sometimes during the first days by passing signs of postoperative hyperfunction.

Together with these morphological signs there are others of thyroid hypofunction: percentage thyroid iodine raised, a low blood iodine content,* low basal metabolism, an increase in the viscosity and globulin content of the plasma.

In the experiments of Artundo and Mazzocco the hypophysectomized dogs without lowered basal metabolism showed a higher thyroid epithelium (3.4 to 4.2 micromillimetres) than those in which the basal metabolism was decreased (less than 3 micra).

In seven hypophysectomized dogs the metabolism sometimes increased after pancreatectomy, but not constantly (the average determinations were 1164, 774, 723, 590, 1040, 682, 888 calories per sqm. per 24 hrs.). In the controls, with pituitary intact, after pancreatectomy the increase was constant (Houssay and Biasotti, 13).

The diminished metabolism noted in hypophysectomized dogs is not as low as that in athyroidism (Table 2 and Graph 2). Therefore in the hypophysectomized animals there is a decrease but not suppression of the thyroid function (10).

If the thyroid is extirpated in a hypophysectomized animal the metabolism is further diminished; but if the pituitary is extirpated in a thyroidectomized animal this additional diminution does not occur, hence it does not seem that the pituitary has an effect of its own on the metabolism (10). (See Table 2.)

These experiments demonstrate that the pituitary in developing and keeping the anatomic and functional state of the thyroid normal indirectly helps to regulate the basal metabolism. Its metabolic action is continuous (tonic) but exercised by way of the thyroid. This conclusion is corrobo-

*The iodine content of blood markedly increases during the first two or three weeks and then it decreases.

TABLE 2

AVERAGE VALUES OF BASAL METABOLISM IN DOGS. (HOUSSAY AND ARTUNDO, 1933)

	Cals./sq. m./day	Dimin. Per Cent	Four Individual Cases	Cals./sq. m./day	
5 normal	804	.....		①	②
7 thyroidectomised	610	−24.1	Normal	662	....
5 hypophysectomised	702	−12.6	Thyrodectomised	565	487
7 hypophysectomised and thyroidectomised	622	−22.2	Thyroidectomised and hypophysectomised	603	475
				③	④
			Hypophysectomised	609	857
			Hypophysectomised and thyroidectomised	472	557

rated by other experiments on the injection of anterior-pituitary lobe extract.

The injection of an alkaline extract of anterior pituitary lobe produces a hyperactivity of the thyroid: the weight of the organ increases, reabsorption of colloid occurs and hypertrophy of the alveolar epithelium, the cells of which enlarge; the iodine content per 100 grams of thyroid diminishes, the blood iodine increases (not in thyroidectomized animals). The basal metabolism rises and the sensitivity to anoxemia is increased, etc.

Table 3 clearly shows the large increase in metabolism produced by the aforementioned extract, which is accompanied by tachycardia, increased

TABLE 3

ARTUNDO AND SOLARI, 1933, WITH ADDITIONAL DATA

Dog	Weight Kg.	Basal Calories/sq. m./day				Pulse Rate per Min.		Dose (1) and Duration of Treatment
		Before Extract	After Extract	Absolute Increase	Percentage Increase	Before Extract	After Extract	
1	8.4	724	1190	466	64	70	92	2 g. 6 days
2	9.2	768	1362	594	77	70	105	2 g. 6 days
		873	1682	809	92	75	128	13 g. 6 days
		....	1257	510	71	....	127	2 g. 6 days
		957	1778	821	85	72	128	13 g. 6 days
3	9.	876	1056	180	20	78	85	2 g. 6 days
		751	982	231	30	72	86	12.6 g. 6 days
		952	1465	513	54	78	135	12.6 g. 6 days
B	9.8	828	1888	828	128	68	104	4 g. 8 days
		844	1709	865	102	76	110	2 g. 10 days
C	5.4	616	1344	628	101	62	100	2 g. 14 days
D	9.	722	1300	578	80	72	125	2 g. 7 days
2b	9.6	873	1692	819	93	70	140	13 g. 5 days
4	9.	738	1450	712	96	76	100	12.6 g. 6 days

(1) In g. of fresh bovine anterior pituitary prepared as alkaline extract given intraperitoneally.

pulmonary ventilation and frequently a slight rise in temperature of some tenths of a degree (3).

This metabolic increase is seen in dogs possessing thyroids (normal or hypophysectomized*) but does not occur or is very slight in thyroidecto-

*In these the thyroid hypertrophy occurred more slowly but the thyroids were atrophied at the beginning.

TABLE 4

INCREASE IN METABOLISM (IN CALS/SQ. M./DAY) PRODUCED BY DAILY INTRAPERITONEAL INJECTIONS OF 10 CC. ALKALINE ANTERIOR PITUITARY EXTRACT (1 CC.=0.2 G. FRESH LOBE) IN DOGS 6-12 KG. (HOUSSAY AND ARTUNDO, 1933)

Normals	Duration of Treatment	Thyroidectomised	Duration of Treatment	Thyroidectomised Hypophysectomised	Duration of Treatment
Calories	Days	Calories	Days	Calories	Days
+466	6	+373	6	+ 70	6
+594	6	+290	6	+262	6
+510	6	+140	6	+350	6
+180	6	− 86	6	− 10	6
+578	7			−170	6
+865	10			−140	6
+628	14				
+628	14				

mized animals (thyroidectomized or thyrohypophysectomized) (Table 4). The slight increase which sometimes occurs in thyroidectomized animals might be due to an impurity in the extract used or to an action of its own, which in any case is inconstant and additional (11). With purer extracts this point will possibly be cleared up.

TABLE 5

AVERAGE INCREASE IN METABOLISM PRODUCED BY 300 G. MEAT, IN CALS/SQ. M./DAY

	Absolute Increase		Percentage Increase	
	2 Hours	5 Hours	2 Hours	5 Hours
	Normal Dogs			
Artundo (1930), 6 dogs	218	396	27	48
Mazzocco (1932), 9 dogs	218	216	25	24
Houssay and Artundo (1933), 5 dogs	215	220	27	28
Average	217	271	26	32
	Hypophysectomised Dogs			
Artundo (1930), 6 dogs	273	388	34	35
Mazzocco (1932), 9 dogs	268	255	39	56
Houssay and Artundo (1933), 5 dogs	215	220	27	28
Average	261	286	34	42
	Dogs With Lesion of Tuber			
Mazzocco (1932), 5 dogs	289	362	36	45
	Thyroidectomised Dogs			
Houssay and Artundo (1933), 6 dogs	161	179	18	20
4 dogs after 6 days treatment with A. L. E.	133	150	14	16
	Thyrohypophysectomised Dogs			
Houssay and Artundo (1933), 7 dogs	144	140	19	19
4 dogs after 6 days treatment with A. L. E.	125	192	17	26

Hours after the meat feeding.

The specific dynamic action in the hypophysectomized animals is not less than in the controls, as has been shown in 20 dogs in our Institute (Artundo, 2; Mazzocco, 17; Houssay and Artundo, 12). In thyroidectomized and thyrohypophysectomized on an average it is slightly less (Houssay and Artundo, 10). Table 5 shows that the thyroid has some influence. The anterior pituitary lobe extract did not cause an increase in the specific dynamic action in the said animals.

Up to the present the basal metabolism has been determined in 22 dogs with lesions of the posterior part of the tuber cinereum, produced in 11 by caustic injections (Grafe and collaborators, 21) and in 11 by galvanic cautery (5 dogs, Mazzocco, 17; 6 dogs, Solari, unpublished results). Grafe and his collaborators found that eight of the 11 dogs in their series had lowered metabolism (average —26 per cent) and 3 were unchanged. The decrease was preceded in some cases by an initial transitory increase. Of the 11 dogs studied in this Institute six had normal metabolism and in five it was lowered. In both groups there was frequently found destruction of the posterior lobe but the anterior lobe was intact or only partially injured. The dogs with low metabolism showed great adiposity and genital atrophy. The mechanism of this lowering of the metabolism is not yet clear, but in several cases there was no epithelial atrophy in the thyroids. These points have been the object of special study by Solari, the results of which will be published later.

SUMMARY

The analysis of the influence of the hypophysis on basal metabolism in one single species (the dog) has received particular attention in our Institute (1930-1933). Hypophysectomy as a rule decreased the basal metabolism to about —16 per cent (22 of 27 dogs). This decrease is due to the anatomical (flattened epithelium, colloid more dense and devoid of vacuoles, and increased iodine content, etc.) and functional hypothyroidism induced by hypophysectomy. Dogs in which the basal metabolism did not decrease showed only a minor degree of atrophy of the thyroid epithelium.

Pancreatectomy produces either no or little increase of the basal metabolism in hypophysectomized dogs, whereas a definite increase is observed in dogs whose hypophysis has not been removed.

Hypophysectomized animals show a decrease but not a total abolition of the thyroid secretion as shown by the fact that thyroidectomy further decreases the basal metabolism (from —12 per cent when hypophysectomized only, to —22 per cent when the thyroid gland was removed in a second operation), thereby equalling the condition of animals from which the thyroid alone is removed (—24 per cent of normal).

Hypophysectomy in thyroidectomized dogs does not produce any further decrease of their basal metabolism. This shows that the hypophysis has no action of its own on the basal metabolism.

Injury of the tuber cinereum often decreases the basal metabolism (14 of 22 dogs showed such decrease) even when there is no sign of atrophy of the thyroid gland.

Alkaline extracts of the anterior lobe of the hypophysis produce hyperthyroidism and strongly increase the basal metabolism. Such an increase is wanting altogether or else is only slight in absence of the thyroid gland.

The specific dynamic action has been found normal in 20 hypophysectomized dogs studied in our Institute. This does not mean that the case must be the same in other species. In dogs lacking both hypophysis and thyroid the specific dynamic action is lower than in control animals.

The hypophysis has an indirect tonic action on metabolism through its influence in developing and maintaining the thyroid gland.

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